SEQUENCE LISTING

(1) GENERAL INFORMATION

(i) APPLICANT: Wei-Wu He, Kristine K. Kikly, Vishva M. Dixit, Steven M. Ruben

(ii) TITLE OF THE INVENTION: INTERLEUKIN-1 BETA CONVERTING ENZYME LIKE APOPTOSIS PROTEASE-6

(iii) NUMBER OF SEQUENCES: 9

(iv) CORRESPONDENCE ADDRESS:
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- (E) COUNTRY: USA
- (F) ZIP: 19406-2799

(v) COMPUTER READABLE FORM:
- (A) MEDIUM TYPE: Diskette
- (B) COMPUTER: IBM Compatible
- (C) OPERATING SYSTEM: DOS
- (D) SOFTWARE: FastSEQ Version 1.5

(vi) CURRENT APPLICATION DATA:
- (A) APPLICATION NUMBER: UNKNOWN
- (B) FILING DATE: HEREWITH
- (C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:
- (A) APPLICATION NUMBER: 60/018,961
- (B) FILING DATE: 05 JUNE 1996

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- (A) APPLICATION NUMBER: 60/017,949
- (B) FILING DATE: 20 May 1996

(viii) ATTORNEY/AGENT INFORMATION:

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 416 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE: N-terminal
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

```
Met Asp Glu Ala Asp Arg Arg Leu Leu Arg Arg Cys Arg Leu Arg Leu
 1               5                  10                  15
Val Glu Glu Leu Gln Val Asp Gln Leu Trp Asp Val Leu Leu Ser Arg
            20                  25                  30
Glu Leu Phe Arg Pro His Met Ile Glu Asp Ile Gln Arg Ala Gly Ser
        35                  40                  45
Gly Ser Arg Arg Asp Gln Ala Arg Gln Leu Ile Ile Asp Leu Glu Thr
    50                  55                  60
Arg Gly Ser Gln Ala Leu Pro Leu Phe Ile Ser Cys Leu Glu Asp Thr
65                  70                  75                  80
Gly Gln Asp Met Leu Ala Ser Phe Leu Arg Thr Asn Arg Gln Ala Gly
                85                  90                  95
Lys Leu Ser Lys Pro Thr Leu Glu Asn Leu Thr Pro Val Val Leu Arg
            100                 105                 110
Pro Glu Ile Arg Lys Pro Glu Val Leu Arg Pro Glu Thr Pro Arg Pro
        115                 120                 125
Val Asp Ile Gly Ser Gly Gly Phe Gly Asp Val Gly Ala Leu Glu Ser
    130                 135                 140
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Leu Arg Gly Asn Ala Asp Leu Ala Tyr Ile Leu Ser Met Glu Pro Cys
145                 150                 155                 160
Gly His Cys Leu Ile Ile Asn Asn Val Asn Phe Cys Arg Glu Ser Gly
                165                 170                 175
Leu Arg Thr Arg Thr Gly Ser Asn Ile Asp Cys Glu Lys Leu Arg Arg
            180                 185                 190
Arg Phe Ser Ser Leu His Phe Met Val Glu Val Lys Gly Asp Leu Thr
        195                 200                 205
Ala Lys Lys Met Val Leu Ala Leu Leu Glu Leu Ala Arg Gln Asp His
    210                 215                 220
Gly Ala Leu Asp Cys Cys Val Val Val Ile Leu Ser His Gly Cys Gln
225                 230                 235                 240
Ala Ser His Leu Gln Phe Pro Gly Ala Val Tyr Gly Thr Asp Gly Cys
                245                 250                 255
Pro Val Ser Val Glu Lys Ile Val Asn Ile Phe Asn Gly Thr Ser Cys
            260                 265                 270
Pro Ser Leu Gly Gly Lys Pro Lys Leu Phe Phe Ile Gln Ala Cys Gly
        275                 280                 285
Gly Glu Gln Lys Asp His Gly Phe Glu Val Ala Ser Thr Ser Pro Glu
    290                 295                 300
Asp Glu Ser Pro Gly Ser Asn Pro Glu Pro Asp Ala Thr Pro Phe Gln
305                 310                 315                 320
Glu Gly Leu Arg Thr Phe Asp Gln Leu Asp Ala Ile Ser Ser Leu Pro
                325                 330                 335
Thr Pro Ser Asp Ile Phe Val Ser Tyr Ser Thr Phe Pro Gly Phe Val
            340                 345                 350
Ser Trp Arg Asp Pro Lys Ser Gly Ser Trp Tyr Val Glu Thr Leu Asp
        355                 360                 365
Asp Ile Phe Glu Gln Trp Ala His Ser Glu Asp Leu Gln Ser Leu Leu
    370                 375                 380
Leu Arg Val Ala Asn Ala Val Ser Val Lys Gly Ile Tyr Lys Gln Met
385                 390                 395                 400
Pro Gly Cys Phe Asn Phe Leu Arg Lys Lys Leu Phe Phe Lys Thr Ser
                405                 410                 415
```

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1578 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTISENSE: NO

(v) FRAGMENT TYPE:

(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

```
GCCATGGACG AAGCGGATCG GCGGCTCCTG CGGCGGTGCC GGCTGCGGCT GGTGGAAGAG     60
CTGCAGGTGG ACCAGCTCTG GGACGTCCTG CTGAGCCGCG AGCTGTTCAG GCCCCATATG    120
ATCGAGGACA TCCAGCGGGC AGGCTCTGGA TCTCGGCGGG ATCAGGCCAG GCAGCTGATC    180
ATAGATCTGG AGACTCGAGG GAGTCAGGCT CTTCCTTTGT TCATCTCCTG CTTAGAGGAC    240
ACAGGCCAGG ACATGCTGGC TTCGTTTCTG CGAACTAACA GGCAAGCAGG AAAGTTGTCG    300
AAGCCAACCC TAGAAAACCT TACCCCAGTG GTGCTCAGAC CAGAGATTCG CAAACCAGAG    360
GTTCTCAGAC CGGAAACACC CAGACCAGTG GACATTGGTT CTGGAGGATT CGGTGATGTC    420
GGTGCTCTTG AGAGTTTGAG GGGAAATGCA GATTTGGCTT ACATCCTGAG CATGGAGCCC    480
TGTGGCCACT GCCTCATTAT CAACAATGTG AACTTCTGCC GTGAGTCCGG GCTCCGCACC    540
CGCACTGGCT CCAACATCGA CTGTGAGAAG TTGCGGCGTC GCTTCTCCTC GCTGCATTTC    600
ATGGTGGAGG TGAAGGGCGA CCTGACTGCC AAGAAAATGG TGCTGGCTTT GCTGGAGCTG    660
GCGCGGCAGG ACCACGGTGC TCTGGACTGC TGCGTGGTGG TCATTCTCTC TCACGGCTGT    720
CAGGCCAGCC ACCTGCAGTT CCCAGGGGCT GTCTACGGCA CAGATGGATG CCCTGTGTCG    780
GTCGAGAAGA TTGTGAACAT CTTCAATGGG ACCAGCTGCC CCAGCCTGGG AGGGAAGCCC    840
AAGCTCTTTT TCATCCAGGC CTGTGGTGGG GAGCAGAAAG ACCATGGGTT TGAGGTGGCC    900
TCCACTTCCC CTGAAGACGA GTCCCCTGGC AGTAACCCCG AGCCAGATGC CACCCCGTTC    960
CAGGAAGGTT TGAGGACCTT CGACCAGCTG GACGCCATAT CTAGTTTGCC CACACCCAGT   1020
GACATCTTTG TGTCCTACTC TACTTTCCCA GGTTTTGTTT CCTGGAGGGA CCCCAAGAGT   1080
GGCTCCTGGT ACGTTGAGAC CCTGGACGAC ATCTTTGAGC AGTGGGCTCA CTCTGAAGAC   1140
CTGCAGTCCC TCCTGCTTAG GGTCGCTAAT GCTGTTTCGG TGAAAGGGAT TTATAAACAG   1200
ATGCCTGGTT GCTTTAATTT CCTCCGGAAA AAACTTTTCT TTAAAACATC ATAAGGCCAG   1260
GGCCCCTCAC CCTGCCTTAT CTTGCACCCC AAAGCTTTCC TGCCCCAGGC CTGAAAGAGG   1320
CTGAGGCCTG GACTTTCCTG CAACTCAAGG ACTTTGNAGC CGGCACAGGG TCTGCTCTTT   1380
CTCTGCCAGT GACAGACAGG CTCTTAGCAG CTTCCAGATT GACGACAAGT GCTGAACAGT   1440
GGAGGAAGAG GGACAGATGA ATGCCGTGGA TTGCACGTGG NCTCTTGAGC AGTGGCTGGT   1500
CCAGGGCTAG TGACTTGGTG TCCCATGATC CCTGTGTTGG TCTCTAGGAG CAGGGATTAA   1560
CCTCTGCACT ACTGACAT                                                 1578
```

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 639 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE:
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```
CTGACTGCCA AGAAAATGGT GCTGGCTTTG CTGGAGCTGG CGCGGCAGGA CCACGGTGCT     60
CTGGACTGCT GCGTGGTGGT CATTCTCTCT CACGGCTGTC AGGCCAGCCA CCTGCAGTTC    120
CCAGGGGCTG TCTACGGCAC AGATGGATGC CCTGTGTCGG TCGAAAAGAT TGTGAACATC    180
TTCAATGGGA CCAGCTGCCC CAGCCTGGGA GGGAAGCCCA AGCTCTTTTT CATCCAGGCC    240
TGTGGTGGGG AGCAGAAAGA CCATGGGTTT GAGGTGGCCT CCACTTCCCC TGAAGACGAG    300
TCCCCTGGCA GTAACCCCGA GCCAGATGCC ACCCCGTTCC AGGAAGGTTT GAGGACCTTC    360
GACCAGCTGG ACGCCATATC TAGTTTGCCC ACACCCAGTG ACATCTTTGT GTCCTACTCT    420
ACTTTCCCAG GTTTTGTTTC CTGGAGGGAC CCCAAGAGTG GCTCCTGGTA CGTTGAGACC    480
CTGGACGACA TCTTTGAGCA GTGGGCTCAC TCTGAAGACC TGCAGTCCCT CCTGCTTAGG    540
GTCGCTAATG CTGTTTCGGT GAAAGGGATT TATAAACAGA TGCCTGGTTG CTTTAATTTC    600
CTCCGGAAAA AACTTTTCTT TTAAAACATC ATAAGGCAG                            639
```

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 203 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE: N-terminal
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```
Met Val Leu Ala Leu Leu Glu Leu Ala Arg Gln Asp His Gly Ala Leu
 1               5                  10                  15
Asp Cys Cys Val Val Val Ile Leu Ser His Gly Cys Gln Ala Ser His
            20                  25                  30
Leu Gln Phe Pro Gly Ala Val Tyr Gly Thr Asp Gly Cys Pro Val Ser
        35                  40                  45
Val Glu Lys Ile Val Asn Ile Phe Asn Gly Thr Ser Cys Pro Ser Leu
    50                  55                  60
Gly Gly Lys Pro Lys Leu Phe Phe Ile Gln Ala Cys Gly Gly Glu Gln
```

```
65                  70                  75                  80
Lys Asp His Gly Phe Glu Val Ala Ser Thr Ser Pro Glu Asp Glu Ser
                85                  90                  95
Pro Gly Ser Asn Pro Glu Pro Asp Ala Thr Pro Phe Gln Glu Gly Leu
            100                 105                 110
Arg Thr Phe Asp Gln Leu Asp Ala Ile Ser Ser Leu Pro Thr Pro Ser
        115                 120                 125
Asp Ile Phe Val Ser Tyr Ser Thr Phe Pro Gly Phe Val Ser Trp Arg
    130                 135                 140
Asp Pro Lys Ser Gly Ser Trp Tyr Val Glu Thr Leu Asp Asp Ile Phe
145                 150                 155                 160
Glu Gln Trp Ala His Ser Glu Asp Leu Gln Ser Leu Leu Leu Arg Val
                165                 170                 175
Ala Asn Ala Val Ser Val Lys Gly Ile Tyr Lys Gln Met Pro Gly Cys
            180                 185                 190
Phe Asn Phe Leu Arg Lys Lys Leu Phe Phe Met
        195                 200
```

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 34 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE:
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

GAACGGGGTA CCGCCATGGA CGAAGCGGAT CGGC 34

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE:
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

TGCTCTAGAT TAGTGGTGGT GGTGGTGGTG TGATGTTTTA AAGAAAAGTT TTTTCCGGAG 60

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 41 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE:
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

AAGCTCTTTT TCATCCAGGC CGCGGGTGGG GAGCAGAAGA C 41

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE:
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

GTCTTTCTGC TCCCCACCCG CGGCCTGGAT GAAAAAAGC 39

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 66 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE:
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

TGCTCTAGAT TACTTGTCAT CGTCGTCCTT GTAGTCTGAT GTTTTAAAGT TAAGTTTTTT 60
CCGGAG 66

What is claimed is:

1. An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide having at least a 70% identity to a polynucleotide encoding a polypeptide comprising amino acids of SEQ ID NO: 1;

(b) a polynucleotide which is complementary to the polynucleotide of (a); and

(c) a polynucleotide comprising at least 15 bases of the polynucleotide of (a) or (b).

2. The polynucleotide of Claim 1 wherein the polynucleotide is DNA.

3. The polynucleotide of Claim 1 wherein the polynucleotide is RNA.

4. The polynucleotide of Claim 2 which encodes a polypeptide comprising amino acid set forth in SEQ ID NO: 1.

5. An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide having at least a 70% identity to a polynucleotide encoding the same mature polypeptide expressed by the human DNA in SEQ ID NO: 2;

(b) a polynucleotide complementary to the polynucleotide of (a); and

(c) a polynucleotide comprising at least 15 bases of the polynucleotide of (a) or (b).

6. A vector comprising the DNA of Claim 2.

7. A host cell comprising the vector of Claim 6.

8. A process for producing a polypeptide comprising: expressing from the host cell of Claim 7 a polypeptide encoded by said DNA.

9. A process for producing a cell which expresses a polypeptide comprising transforming or transfecting the cell with the vector of Claim 6 such that the cell expresses the polypeptide encoded by the human cDNA contained in the vector.

10. A polypeptide comprising an amino acid sequence which is at least 70% identical to amino acid set forth in SEQ ID NO: 1.

11. A polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 1.

12. An agonist to the polypeptide of Claim 10.

13. An antibody against the polypeptide of Claim 10.

14. An antagonist which inhibits the activity of the polypeptide of Claim 10.

15. A method for the treatment of a patient having need of ICE LAP-6 comprising: administering to the patient a therapeutically effective amount of the polypeptide of Claim 10.

16. The method of Claim 15 wherein said therapeutically effective amount of the polypeptide is administered by providing to the patient DNA encoding said polypeptide and expressing said polypeptide *in vivo*.

17. A method for the treatment of a patient having need to inhibit ICE LAP-6 polypeptide comprising: administering to the patient a therapeutically effective amount of the antagonist of Claim 14.

18. A process for diagnosing a disease or a susceptibility to a disease related to expression of the polypeptide of Claim 10 comprising: determining a mutation in the nucleic acid sequence encoding said polypeptide.

19. A diagnostic process comprising: analyzing for the presence of the polypeptide of Claim 10 in a sample derived from a host.

20. A method for identifying compounds which bind to and activate or inhibit a receptor for the polypeptide of Claim 10 comprising: contacting a cell expressing on the surface thereof a receptor for the polypeptide, said receptor being associated with a second component capable of providing a detectable signal in response to the binding of a compound to said receptor, with a compound to be screened under conditions to permit binding to the receptor; and determining whether the compound binds to and activates or inhibits the receptor by detecting the presence or absence of a signal generated from the interaction of the compound with the receptor.

ABSTRACT OF THE DISCLOSURE

Human ICE LAP-6 polypeptides and DNA (RNA) encoding such ICE LAP-6 and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such ICE LAP-6 for the treatment of a susceptibility to viral infection, tumorogenesis and to diseases and defects in the control embryogenesis and tissue homeostasis, and the nucleic acid sequences described above may be employed in an assay for ascertaining such susceptibility. Antagonists against such ICE LAP-6 and their use as a therapeutic to treat Alzheimer's disease, Parkinson's disease, rheumatoid arthritis, septic shock, sepsis, stroke, chronic inflammation, acute inflammation, CNS inflammation, osteoporosis, ischemia reperfusion injury, cell death associated with cardiovascular disease, polycystic kidney disease, apoptosis of endothelial cells in cardiovascular disease, degenerative liver disease, MS, ALS, cererbellar degeneration, ischemic injury, myocardial infarction, AIDS, myelodysplastic syndromes, aplastic anemia, male pattern baldness, and head injury damage are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding the interleukin-1 beta converting enzyme apoptosis proteases and for detecting altered levels of the polypeptide in a host.